

09/767,215

Set	Items	Description
S1	277	AU='BERTIN J' OR AU='BERTIN J.'
S2	63	AU='BERTIN JOHN' OR AU='BERTIN JOHN J'
S3	340	S1 OR S2
S4	1850	CARD(W) 14
S5	338541	CARD
S6	0	CAPASE(W) RECRUITMENT(W) DOMAIN? ?
S7	5	S3 AND S4
S8	4	RD (unique items)
S9	1503	S4 NOT PY>2000
S10	1495	RD (unique items)
S11	564	CASPASE(W) RECRUITMENT(W) DOMAIN
S12	264	S11 NOT PY>2000
S13	91	RD (unique items)
S14	424661	APOPTOSIS
S15	1585	S10 OR S13
S16	80	S14 AND S15
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16/3,AB/26 (Item 26 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

10040651 99040667 PMID: 9823333

**Identification and characterization of murine caspase-14, a new member of the caspase family.**

Ahmad M; Srinivasula S M; Hegde R; Mukattash R; Fernandes-Alnemri T; Alnemri E S

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We report here the identification and characterization of a new member of the mouse caspase family, named caspase-14. Northern blot analysis of mRNA from various tissues with caspase-14-specific probe showed a major transcript size of approximately 2.4 kb and variant transcripts of 2.0 kb and 1.5 kb. The major transcript is detected mainly in the liver and to a lesser extent in the brain and kidney. Caspase-14 cDNA encodes a 257-amino acid-long protein that has significant homology to other members of the caspase family. Like other caspases, caspase-14 has a conserved active site, pentapeptide QACRG. However, it lacks an NH2-terminal prodomain or a **caspase recruitment domain**, suggesting that it could be a downstream caspase that depends on other initiator caspases for activation. Consistent with this, procaspase-14 can be processed in vitro by the death receptor-associated caspase-8 and caspase-10 but not other caspases, and in vivo after stimulation of cells with anti-Fas agonist antibody or Tumor Necrosis Factor-Related **Apoptosis** Inducing Ligand. Furthermore, procaspase-14 can be cleaved by granzyme B. These observations suggest that caspase-14 may play a role in death receptor and granzyme B-induced **apoptosis**.

16/3,AB/33 (Item 4 from file: 5)  
DIALOG(R) File 5:Biosis Previews(R)  
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**Structural analysis of caspase recruitment domains (CARDs).**

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**The CARD domain: A new apoptotic signalling motif**

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The first steps of FAS-induced or tumor-necrosis factor (TNF)-induced **apoptosis** require the transmission of the apoptotic signal from the plasma membrane receptors to caspases, a group of interleukin-1 beta -converting enzyme (ICE)-related proteases, which are activated by proteolytic cleavage usually performed by other caspases. The apoptotic signal is frequently mediated by the association of proteins containing homology domains of the same class. By application of the generalized profile technique, a sensitive method for sequence database searches, we detected regions with highly significant similarity to the RAIDD/ICH-1 amino-terminal domain in a number of additional proteins involved in apoptotic signalling. The biological role of proteins containing this domain allows the prediction of a network of interactions necessary to recruit caspases to the receptor complexes signalling **apoptosis**. We therefore propose the name CARD (for **caspase recruitment domain**). Initial profiles were constructed from an alignment of the amino-terminal regions of RAIDD, ICH-1 and Ced-3. Two iteration cycles of profile searches identified with high significance matches in other caspases (Mch6, ICE), in two cellular homologues of the viral **apoptosis** inhibitor IAP (c-IAP1, c-IAP2), in the uncharacterised ORF E10 from the herpesvirus EHV2, and in a hypothetical protein from rat. Because of their known involvement in apoptotic signalling, we also accepted the nematode cell death protein Ced-4 and mammalian caspase-4 (ICH-2/ICH-3) despite their slightly subsignificant profile score (rank 3 and rank 12 in the list of non-significant scores, respectively). An alignment of representative proteins containing CARD domains is shown in Fig. 1a. All characterized proteins found to contain the CARD domain have been reported to act in apoptotic signalling. ICH-1, Ced-3, ICE and Mch6 all belong to the caspase family. In these proteins, the CARD domain is a part of the amino-terminal propeptide. (DBO)  
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